blood advances

Race and insurance: real-world insights on CAR-T outcomes

Nausheen Ahmed[1] and Natalie S. Grover[2,3]

[1]Division of Hematologic Malignancies and Cellular Therapeutics, University of Kansas Cancer Center, Kansas City, KS; [2]Lineberger Comprehensive Cancer Center and [3]Division of Hematology, Department of Medicine, The University of North Carolina at Chapel Hill, Chapel Hill, NC

Comment on Karmali et al, page 2592

In this issue of *Blood Advances*, Karmali et al[1] identified the impact of racial and insurance disparities on survival outcomes in patients with diffuse large B-cell lymphoma (DLBCL)/transformed follicular lymphoma (tFL) treated with chimeric antigen receptor T-cell therapy (CAR-T) as a standard of care and in clinical trials.

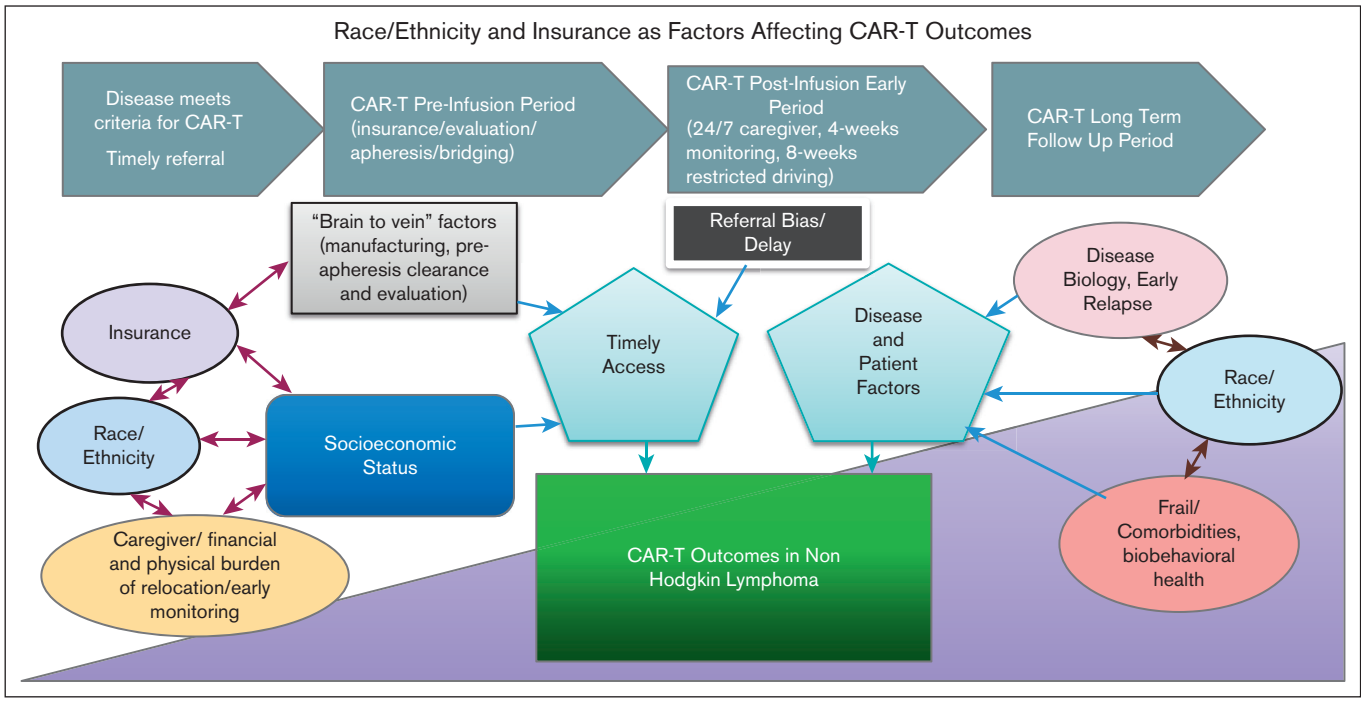
CD19-directed CAR-Ts have altered the treatment landscape for patients with DLBCL with the recent ZUMA-7 trial demonstrating an overall survival (OS) benefit in the second-line setting.[2] However, CAR-T is also associated with unique logistical challenges, including, but not limited to, the requirement of receipt at a specialized center, toxicity monitoring, and high out-of-pocket cost, which may lead to disparities in access both in the context of a clinical trial as well as the standard of care (see figure).

Although most reports describe the access issue, this study uniquely focused on outcomes based on race and payer type. This was a multicenter retrospective study evaluating patients with DLBCL/tFL treated with CD19 CAR T cells between 2015 and 2021 at 13 US academic centers across the country. Race had an impact on the median progression-free survival (PFS) but not OS. The median PFS for Caucasians was 11.5 months compared with 3.5 months for African Americans (AAs) and 2.7 months for Asians. AAs had significantly worse PFS than Caucasians. In this cohort, there were no differences in the time from diagnosis or relapse to CAR-T, number of prior lines of therapy, use of bridging therapy, toxicity, or post–CAR-T progression salvage therapy between racial groups.

Medicare coverage was associated with improved PFS and OS compared with other coverages, which included Medicaid, private insurance, and self-pay. However, when compared individually, the difference was not statistically significant between Medicare and private insurance, so it was likely driven more by Medicaid and self-pay groups. Another study investigating cancer outcomes based on insurance type found inferior survival in patients with Medicaid or without insurance.[3] However, in a study by Karmali et al, other confounding factors may have been present. The authors hypothesized that this may have been related to the fact that Medicare patients in this cohort seemed to have a less aggressive disease, as suggested by the longer time from diagnosis to CAR-T. Larger studies are needed to further explore and explain the differences in outcomes according to insurance type.

One important question is the etiology of these differences and whether it is related to biologic, socioeconomic, structural factors, or a combination of these. It is important to note that the sample size across different payer and racial categories is small; therefore, larger studies are needed to confirm these findings and further investigate the root causes of these disparities.

Another key point highlighted by this study is the low rates of minorities receiving CAR-T which matches what was seen in clinical trials and underscores the disparities in access to CAR T cells in the real world. There are limited data on how race and social determinants of health, including insurance status, may impact treatment outcomes. Minorities have been underrepresented in CAR-T clinical trials, with non-Hispanic Blacks comprising only 5% of patients globally and 6.4% of US patients on ZUMA-7.[2] In the study by Karmali et al, of 466 patients, 406 (87%) patients were Caucasian, 34 (7%) were AA, 26 (6%) were Asian, and 9 (2%) were Hispanic. Although almost three-quarters of the patients received CAR-T outside of a clinical trial, there remains a disproportionate underrepresentation of AA, which is also seen in other reports.[4] In a real-world analysis of 1389 patients receiving axicabtagene ciloleucel for DLBCL, 81% were White, 5% were AA, 6% were Asian, and 11% were Hispanic. There were lower response rates in AA patients than in Caucasian patients but there were no differences in survival or toxicity. A key question is whether the most significant disparities are at the time of consideration for



Race/ethnicity and insurance as factors affecting CAR-T outcomes. This diagram depicts the complex interplay between multiple factors including race/ethnicity and insurance status, which contribute to access to therapy and posttreatment outcomes.

CAR-T, given the lower number of minorities treated, which cannot be explained alone by a lower incidence of DLBCL. Another study investigated the association between socioeconomic factors and the receipt of CAR-T in patients with hematologic malignancies.[5] AA patients, uninsured patients, patients with Medicare, and patients with lower socioeconomic status, defined as the median household income for zip code, were less likely to receive CAR-T. In addition, almost one-third of patients traveled over 2 hours for treatment and most of these patients had a higher socioeconomic status, highlighting the barriers for many patients to be able to receive this therapy, including the need for travel, lodging, and finding a caregiver.[6] These disparities are also seen in access to CAR-T clinical trials. A recently published analysis of available CAR-T and bispecific clinical trials for DLBCL found that 20 states in the United States had no open CAR-T or bispecific trials and only one-third of AA lived in a county with an available trial.[7] Disparities in outcomes for patients receiving CAR-T are likely just the tip of the iceberg and do not account for the many patients who are candidates for CAR-T but are either not referred or unable to be treated.[8] Larger studies are needed to tease out the role of race vs other social determinants of health, such as distance to the treatment center, income, and available social support, in CAR-T outcomes.

The logical next question is to define biologic and biobehavioral differences that affect responses by race, ethnicity, and socioeconomic strata, and determine strategies to reduce and eliminate disparities in outcomes after treatment with CAR-T. Crucial steps include advocacy to promote and educate minority and underserved groups, increasing resources for patients and their caregivers, and educating community oncologists to encourage early referrals.[6] Given the large number of patients who live far away from a CAR-T treatment center, investigation of hybrid care models and collaborations between CAR-T physicians and community oncologists to allow patients to receive some of their care closer to home could help reduce the physical and financial burden.[9,10] Finally, collaborations of key stakeholders such as patient advocacy groups, community oncology practices, leading national societies for cellular therapy, and governmental organizations, will be important to reduce disparities.

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